

## REMARKS

After amendment, claims 63-93 remain pending in the present application, claims 1-62 having been cancelled pursuant to the filing of the instant application and the Examiner's issuance of a restriction requirement. Note that claims 63-92 are directed to compounds and pharmaceutical compositions based upon same and claim 93 is directed to the synthesis/process of producing a single chemical compound. No amendment was deemed necessary to place these claims in condition for allowance because the compound claims are free of the prior art and the process claim 93 is directed to a compound which is neither disclosed nor suggested by the cited art and is non-obvious over same. It is anticipated that Applicants will file one or more divisional applications directed to cancelled subject matter. No new matter has been added by way of this amendment.

The Examiner variously rejected and/or objected to previously filed claims 63-89 and 93 (claim 90-92 were the only claims considered allowable) under 35 U.S.C. §102 or §103 for the reasons which are stated in the office action on pages 2-4. Applicants respectfully submit that the claims as amended and presented do not raise issues under 35 U.S.C. §102 or §103 and should be considered allowable for the reasons which are stated hereinbelow. Applicants address each of the Examiner's rejections and consider them moot for the reasons which are set forth in the sections which follow.

### The 35 USC §102 Rejections

The Examiner has rejected claims 63, 88 and 89 as being anticipated by Trigo, et al., *J. Heterocyclic Chem.* (1980) 17, pp. 69-72 ("Trigo") for the reasons which are stated in the office action on page 2. In particular, the Examiner indicates that Trigo teaches claims 5-7 on page 69, in scheme I, which correspond to claims 1, 26, 28 and 55-58 (formula A where B and C form a ring,  $n=2$  and  $R_5 = OH$ ). Applicants respectfully traverse the Examiner's rejection.

The present invention, which, in its broadest terms is claimed in claim 63 is directed to the specific compounds as claimed. Applicants have carefully reviewed Trigo, Scheme1 and compounds 5-7 and have concluded that Trigo does not anticipate the present invention. Note that in the present compounds, there are methoxy groups in the distal (i.e., the uppermost and lowermost positions on the phenyl groups). Because of the nature of the stereochemistry, both the uppermost and lowermost groups on the phenyl groups of the ring are substituted with methoxy groups. Trigo, in contrast, contains only a hydrogen at the lowermost position of the phenyl ring, not a methoxy group. Consequently, Trigo cannot possibly anticipate claims 63, 88 or 89.

Note that in claim 1, when B and C form a ring, OR<sup>1</sup> and OR<sup>2</sup> are found in set positions at the uppermost and lowermost positions of the two phenyl rings. Although the claimed compound without ring formation contains rotamers (where compounds are formed by rotation about a single bond), the rotamers could not form a ring between B and C and therefore the chemistry about B and C must be fixed, thus resulting in ring compounds which contain methoxy groups in positions as set forth in the compound of claim 64. Inasmuch as the compound of claim 64 is not anticipated by Trigo, the compound of claim 63 cannot be anticipated by Trigo. Applicants respectfully request the Examiner withdraw his rejection of the claims based upon the disclosure of Trigo.

The Examiner has also rejected claims 63, 88 and 89 as being anticipated by Petit, et al., *J. Natural Products* (1984) 47, pp. 913-919 ("Petit") for the reasons which are stated in the office action on page 2. It is the Examiner's position that claims 63, 88 and 89 and in particular, claimed compounds of formula A wherein B and C form a ring, n=1 and R5= OH are anticipated by compounds 1a, 1b, 2, 3, and 4a-4c on page 915. Applicants respectfully traverse the Examiner's rejection.

The compounds of Petit do not contain hydroxyl or alkoxy (methoxy) groups in the distal position as are required by the presently claimed compounds. In each of the disclosed compounds of Petit cited by the Examiner, at least one hydroxyl or alkoxy group is missing from disclosed compound presented in Petit. Consequently, because of

the non-overlap of disclosed compounds of Petit with the compounds of claims 63, 88 or 89, anticipation is not made out. Applicants respectfully request the Examiner to withdraw his rejection of the instant claims based upon the disclosure of Petit.

The Examiner has also rejected claims 63, 88 and 89 as being anticipated by Saifah, et al., *J. Natural Products* (1983) 46, pp. 352-358 ("Saifah") for the reasons which are stated in the office action on page 3. It is the Examiner's position that compounds 1, 2 and 6a-6c on page 354 of Saifah anticipate claims 63, 88 and 89. Applicants respectfully traverse the Examiner's rejection of the instant application based upon Saifah.

A review of the compounds which are disclosed by Saifah on page 354 evidences that the instant invention is not anticipated by Saifah. Saifah does not disclose compounds which contain hydroxyl or methoxy groups at distal ends of the phenyl groups of the disclosed compounds as in the present invention, and consequently, Saifah cannot be seen as anticipating the present invention.

For the reasons which are set forth in detail hereinabove, it is respectfully submitted that the instant invention is not anticipated by Trigo, Petit or Saifah. Applicants, therefore, respectfully request the Examiner to withdraw his rejection on these grounds.

#### The 35 USC §103 Rejection

The Examiner has rejected claim 93 as being obvious over the combined disclosures of Trigo (referenced above) and Liepa, et al., *J. Chem Comm.* (1977) 22, 826-827 ("Liepa") for the reasons which are set forth in the office action on pages 3-4. Essentially it is the Examiner's view that Trigo teaches a dehydration reaction of 15-OH tyloindicine compounds and Liepa teaches reducing tyloindicine compounds using steps which are similar to those of the method set forth in claim 93. It is the Examiner's view that it would be obvious to one of ordinary skill in the art to use the prior art process steps

as analogous process components which are structurally related in an otherwise known process to obtain the invention of claim 93. Applicants respectfully disagree.

The invention of claim 93 is directed to a method of synthesizing the compound which is specifically claimed using a very specific chemical compound as starting material as claimed and subjecting the starting material to a sulfurane dehydration reaction to produce the intermediate alkene, and the alkene is then subjected to a reduction reaction to reduce the keto group on the five-membered ring to provide the specific compound which is claimed. The invention of claim 93 is not in any way obvious over the disclosure of Trigo, in view of Liepa.

Trigo discloses several compounds on page 69. The starting material, the intermediate compound and endpoint compounds are distinguishable from Trigo, in a number of ways including the substituents on the two phenyl groups, the amount of saturation in the ring system bridging the two phenyl groups and the stereochemistry of the hydroxyl group and hydrogen atoms which bridge the various rings. Further, there is no keto group on a five-membered ring in Trigo. None of these features of the starting material, intermediate alkene or final product is disclosed by Trigo. Secondly, none of the steps which are used in the present invention are disclosed or suggested by Trigo. Indeed, the dehydration reaction proceeds through the use of 70% perchloric acid and cannot be described as a sulfurane dehydration as in the present invention. Thus, Trigo is deficient in failing to disclose the method of claim 93 in a number of specific and important ways.

Liepa does absolutely nothing to cure the deficiencies of Trigo in failing to disclose or suggest the present invention. Liepa does not disclose or suggest the compounds which are specifically used in claim 93, and Liepa does not even use a dehydration reaction but rather relies on a cyclization reaction with simultaneous dehydrogenation to provide an alkene (compounds 13 and 14 on page 827), which alkene is not even at the same position as the alkene which is formed in the process of claim 93. Thus, it is respectfully submitted that Liepa, which does not disclose the starting material,

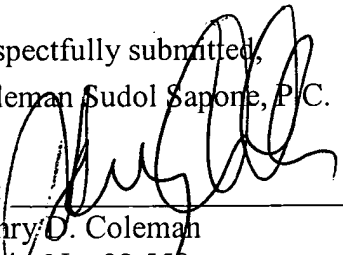
intermediates or dehydration reaction step consistent with the present invention would somehow cure the completely deficient Trigo reference which discloses none of the specific chemical components of claim 93 (starting material, intermediate or final product) or the sulfurane dehydration step or reduction step. In short, a combination of the disclosures of Trigo and Lipea simply does not provide motivation, disclosure or even remote suggestion to produce the present invention as set forth in claim 93. It is respectfully submitted that claim 93 is clearly patentable over the disclosure of Trigo, in view of Liepa.

For the above reasons, the prior art does not anticipate or render obvious the presently claimed invention.

For the above reasons, Applicant respectfully asserts that the claims set forth in the amendment to the application of the present invention are now in compliance with 35 U.S.C. Applicants respectfully submit that the present application is now in condition for allowance and such action is earnestly solicited. Applicants have neither cancelled nor added any claim.

An extension of time of two months and the appropriate fee is submitted herewith.  
If any additional fee is due or any overpayment has been made, please charge/credit  
Deposit Account No. 04-0838.

Respectfully submitted,  
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